Scapuloperoneal Myopathy and Cardiomyopathy with a Novel MYH7 Mutation: A Case Report

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Introduction

Myosin heavy chain 7 (MYH7) gene encodes for myosin heavy chain-beta (MHC-β), which is the major protein comprising thick filaments in cardiac muscle and in slow twitch type 1 fibers of skeletal muscles.[1]

MYH7-related myopathies have variable clinical features, onsets, and are emerging as a group of muscle diseases that affect a wide range of age groups.[11] MYH7 gene mutation-related myopathy has been reported in hypertrophic cardiomyopathy (HCM, MIM # 196200), dilated cardiomyopathy (DCM, MIM # 115200), Laing distal myopathy (MPD1; MIM # 160500), myosin storage myopathy (MSM, MIM # 608358), and congenital fiber type disproportion (CFTD, MIM # 255310).[2-4] Additionally, scapuloperoneal, limb girdle muscle form, multi-mini-core disease with variable cardiac involvement has been reported with MYH7 gene mutations. [13-14]

While individuals with MYH7-related myopathies will present with cardiac or skeletal involvement, it is less common to see cardiac and skeletal involvement co-occurring in a single individual.[2,11] In this case report, we describe a patient with ascending muscular weakness and dilated cardiomyopathy with a heterozygous MYH7 gene mutation.

Case Report

A 66-year old right-handed woman presented to the outpatient Neurology Clinic for evaluation of progressive ascending weakness and dyspnea. The patient first noted lower extremity weakness in her 20s that has slowly progressed to her upper extremities in her 50s. The patient reported an extensive family history of progressive muscular weakness and cardiomyopathy. The patient reported her father passed away from a myocardial infarction 43 years old, and son died from heart failure at 33 years old. Per patient, no further details were known about the cause of death. Patient reported no formal genetic testing has been done for any family members and was not interested in genetic testing despite it being offered at our clinic.

Upon presentation to the Neurology clinic, patient stated she is no longer able to raise her arms above her head, bend to put her shoes on, and has difficulty using her hands. Patient also reported new onset of exertional dyspnea.

Neurological examination of mental status and cranial nerves were intact. On a manual muscle test, patient was unable to raise her arms above her head. Her strength on Medical Research Counsil (MRC) 0/5 strength of deltoids bilaterally, 4/5 strength of triceps and biceps bilaterally, and 3/5 strength at wrist extensors bilaterally. The patient had wasting of the thenar eminences and weak hand grip bilaterally. Furthermore, the patient had a 3/5 strength of hip flexion bilaterally, 3/5 strength of knee flexors and extensors bilaterally, and 1/5 strength of ankle dorsiflexion bilaterally. Reflexes were 1+ bilaterally throughout exam, and the patient had a wide-based, waddling gait. Lastly, high arched feet with hammertoes were noted.

There was no elevation of serum creatinine kinase, and EMG showed myopathic process. Muscle biopsy of the deltoid reported from outside facility revealed myopathic changes with mini cores. Unfortunately, no biopsy images were available from outside institution. The cardiac evaluation included EKG and Echocardiogram. EKG reveals first degree AV block with anterior ischemia. Patient's echocardiogram revealed features of dilated cardiomyopathy, including left ventricular dilation with reduced systolic function and normal wall thickness. The genetic panel was conducted through PerkinElmer Genomics and revealed c.4522_c.4524del (p.Glu1508del) resulting in pathogenic mutation of MYH7, with a scapuloperoneal myopathy and cardiomyopathy phenotype.

Discussion

MYH7, which encodes for myosin heavy chain-beta, plays a crucial role in cardiac contractility and skeletal muscle fibers. Previous studies have reported mutations in the NH globular head, and COOH tail of MYH7 gene resulted in cardiomyopathy and skeletal myopathies, respectively.[5,8] However, research has shown that the location of the mutation and phenotypes do not necessarily correspond. [6-10] Our case report reveals the location of the MYH7 gene mutation is in the COOH tail domain (c.4522_c.4524del: p.Glu1508del) , which resulted in co-occurring scapuloperoneal and dilated cardiomyopathy in an adult patient. Similar to our case report, there has been reported cases of skeletal muscle myopathy with associated cardiomyopathy.[5,7-8,10,15-17]

Specifically, a study by Yüceyar et al has many parallels to the case report we present. [7] One member from the study family reported by Yüceyar had a unique presentation of a

slowly progressive scapuloperoneal type weakness with a normal creatine kinase level. In this individual, Yüceyar reported exertional dyspnea with echocardiogram findings of dilated cardiomyopathy.[7] These unique combination findings were almost identical to the patient described in our case report. However, in contrast to our report, Yüceyar identified a homozygous mutation in MYH7 exon. Of the cases reported with co-occurring skeletal myopathy and cardiomyopathy findings, only two to date were noted to be homozygous.[7-8]

Our case, like the majority of MYH7 mutations with co-occurring skeletal and cardiac myopathies, demonstrated a heterozygous mutation.[5,10,15-17] Furthermore, while our patient's family was not interested in receiving genetic testing, the history of multiple family members affected in each generation is highly suggestive of an autosomal dominant pattern of transmission.

In conclusion, this case report highlights the pertinent family history that is commonly associated with MYH7 mutations. It also illustrates the variability in the phenotypic presentation of this novel mutation. [9-11] While it is still not well understood why different MYH7 mutations result in various phenotypes, we hope that this unique combination of clinical findings will help increase awareness to the broad phenotypic spectrum related to MYH7-myopathies.

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